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Direct Healthcare Professional Communication on the supply of *Fabrazyme®* *(agalsidase beta)*
Update on supply and recommendations on treatment for patients

Dear Healthcare Professional,

Genzyme would like to inform you that **the supply of Fabrazyme (*agalsidase beta*) for the period July through September 2010 will be lower compared to the previous three months**. In this period we can supply approximately half of the quantity that we were able to supply in the period April through June this year. Assuming an average body weight of 60kg, this would allow treating approximately 180 patients at the recommended dose of 1 mg/kg every other week. **There is clearly not enough Fabrazyme to fully address the medical needs of the nearly 600 patients currently receiving Fabrazyme in Europe today.**

As a result of discussions with the EMA, to deal with this shortage, **new temporary treatment recommendations have been agreed**.

For all patients (adults and children):

1. In situations where **alternative treatment is available**:

- Newly identified Fabry patients should not be treated with Fabrazyme for the moment. Treatment with alternative approved treatments (Replagal) should be considered.

- Based on local availability of Enzyme Replacement Therapy for Fabry patients:

  - Patients currently treated with Fabrazyme at the recommended dose of 1 mg/kg every other week should continue on this dosing regimen.
  - Patients treated with a dose of Fabrazyme lower than 1mg/kg every other week should be evaluated for switch to alternative approved treatments (Replagal).

2. In situations where **alternative treatment is not available** or where (continuation of) treatment with Fabrazyme is deemed medically necessary it is important to note that an increase in clinical manifestations indicative of Fabry disease progression has been observed on lowered dose. Pain, cardiac manifestations and deafness are usual manifestations of Fabry disease.

- All patients, especially those with adjusted dose regimens should be under close clinical surveillance. A medical examination, including all relevant clinical parameters, should be performed every two months. It is of the utmost importance to monitor the plasma GL-3 or urinary GL-3 levels, as for the moment the GL-3 level is the most sensitive parameter.

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- Adverse events should continue to be reported in the usual manner and health care professionals are reminded to document batch numbers in the patient record.

Genzyme will continue to provide updates on the production and supply of Fabrazyme.

These are temporary recommendations and do not change the currently approved Product Information for Fabrazyme. The recommendations only apply until the supply problems have been resolved.

Should you require any further information, please contact the Genzyme entity in your country via e-mail xxx or telephone xxx.

Yours sincerely,

C. Geoffrey McDonough, MD.
President, Genzyme Europe